UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/711,101	08/23/2004	George Blanck	1372.183.PRC	5100

21901 7590 02/02/2006

SMITH & HOPEN PA
15950 BAY VISTA DRIVE
SUITE 220
CLEARWATER, FL 33760

EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/711,101	BLANCK ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *4-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/04 & 12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I, claims 1-3 in the reply filed on November 28, 2005 is acknowledged.

Claims 4-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 28, 2005.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specifically, the address of inventor Palubin has been altered.

Specification

The use of the trademark "Metamorph" has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim recites that the method of claim 1 is performed by contacting a target cell with "an RNA inhibitor molecule". This claim is indefinite because the claimed invention is a method of inhibiting mRNA function, thus it is unknown whether the claim is meant to recite that the inhibitor molecules are RNA or if it is meant to recite that the molecule is an RNA inhibitor and includes any molecule that inhibits RNA. For the purposes of examination this claim is interpreted to mean that the molecule is an RNA inhibitor.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 1 is directed to a method of modulating growth of a tumor by contacting the target cell with an inhibitory substance that prevents Oct-1 mRNA function. Claims 2 and 3 limit claim 1 by stating that the inhibitory substance is a vector containing an Oct-1 antisense sequence or an RNA inhibitor molecule.

The claimed invention is directed to methods of modulating tumor growth and thus encompasses use of inhibitors of Oct-1 that increase or decrease tumor growth. The specification describes inhibition of Oct-1 expression using vectors encoding one of five Oct-1 antisense sequences. The specification does not describe the structure of any inhibitory substance that reduces Oct-1 expression and increases tumor growth; the prior art is silent with regard to such substances.

The claims are directed to inhibitory substances that prevent Oct-1 mRNA function. To prevent something is to stop it from occurring. The antisense vectors described reduce Oct-1 mRNA and thus prevent its function to some extent but the specification does not describe the structure of any inhibitors of Oct-1 that completely prevent mRNA function.

The claimed invention encompasses the use of any substance that can inhibit Oct-1 mRNA function from any species. Such inhibitors include antisense oligonucleotides, ribozyme and siRNAs and also include non-nucleic acid inhibitors such as antibodies, small organic molecules and inorganic molecules. Oct-1 is a ubiquitous transcription factor with the gene sequence of numerous species known in

the prior art. The specification describes the administration antisense sequences to Oct-1 for the purpose of western blotting. Two of these vectors were shown to decrease cell growth as compared to a control vector. The structure of the Oct-1 antisense sequences are not disclosed, nor is the species of Oct-1 used disclosed, it is presumed to be human. The specification does not describe antisense sequences directed to Oct-1 from any other species and does not describe the structure of any other type of Oct-1 inhibitor that would inhibit Oct-1 from any species.

Neither the specification nor the prior art describe structures that are representative of the full genus of encompassed compounds that have the function of inhibiting Oct-1. The skilled artisan cannot envision the encompassed modulating agents that prevent Oct-1 mRNA function and decrease or increase tumor growth, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulation of the growth of a tumor by inhibition of Oct-1 mRNA function in a cell *in vitro*, does not reasonably provide enablement for modulation of tumor growth by inhibition of Oct-1 mRNA function in any organism *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is directed to modulation of tumor growth using an inhibitory substance that prevents Oct-1 mRNA function. Such inhibitory substances can be vectors that contain an Oct-1 antisense sequence.

The specification describes western blotting experiments wherein the amount of Oct-1 was quantified after treatment of a human bladder cancer cell line with vectors encoding five antisense sequences. Two of these vectors decreased cell growth as compared to a control vector. The specification does not provide any examples where inhibition of Oct-1 mRNA function led to the modulation of tumor growth in any organism.

Problems related to *in vivo* use of nucleic acids were well known in the art at the time of invention (see for example Opalinska et al. Nature Reviews Drug Discovery, 2002, vol. 1, p. 503-514). Such problems include the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a significant or therapeutic effect.

Opalinska et al. state on page 511

"[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA"

and in column 2 of the same page,

"Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo* in all organisms, with a resultant prevention of Oct-1 mRNA function, as claimed. Due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*, the uptake and biological activity observed *in vitro* would not predictably translate to *in vivo* results. Given the teachings of the prior art, the skilled artisan would not know *a priori* whether introduction of oligonucleotides *in vivo* would result in the oligonucleotide reaching the proper cell in a sufficient concentration and remaining for a sufficient time to provide successful inhibition of expression of a target gene. In fact, the state of the art is such that successful delivery of oligonucleotide sequences *in vivo*, such that the polynucleotide or oligonucleotide provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically.

The specification does not provide the guidance required to overcome the art-recognized unpredictability of using nucleic acids in therapeutic applications in any organism. The teaching of the prior art does not provide that guidance, such that the skilled artisan would be able to practice the claimed therapeutic methods.

Thus, while the specification is enabling for inhibition of Oct-1 mRNA in cells *in vitro*, the specification is not enabling for the broad claims of modulating tumor growth by inhibiting the expression of Oct-1 in any organism as the art of inhibiting gene expression by introducing oligonucleotides into an organism is neither routine nor predictable. The amount of experimentation required is such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore, claims 1-3 are not enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Weiser et al. (Molecular Biology of the Cell 1997, vol. 8, pages 999-1011).

The claimed invention is directed to a method of modulating tumor growth comprising contacting a target cell with an inhibitory substance that prevents Oct-1 mRNA function.

Weiser et al. disclose that heparan sulfate is an inhibitor of Oct-1 expression. Weiser et al. administer this inhibitor to vascular smooth muscle cells, the target cell of their experiment, and observe that Oct-1 mRNA expression is inhibited in the presence of the basement membrane perlecan, specifically the heparan sulfate side chains of perlecan (see page 1005). Although Weiser et al. is silent with regard to modulation of tumor growth, Weiser et al. disclose the step of the claimed method, contacting a target cell with an inhibitory substance that prevents Oct-1 mRNA function, and absent evidence to the contrary the disclosed method would be expected to modulate tumor growth.

Thus, Weiser et al. disclose all limitations of and anticipate claims 1and 3.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Dent et al. (Journal of Biological Chemistry 1991, vol. 266, pages 20888-20892).

The claimed invention is directed to a method of modulating tumor growth comprising contacting a target cell with an inhibitory substance that prevents Oct-1 mRNA function.

Dent et al. disclose that interferon-α is an inhibitor of Oct-1 expression. Dent et al. administer interferon-α to Daudi cells, the target cell of their experiment, and observe that Oct-1 mRNA expression is inhibited. Although Dent et al. is silent with regard to modulation of tumor growth, Dent et al. disclose the step of the claimed method, contacting a target cell with an inhibitory substance that prevents Oct-1 mRNA function, and absent evidence to the contrary the disclosed method would be expected to modulate tumor growth.

Thus, Dent et al. disclose all limitations of and anticipate claims 1and 3.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
January 23, 2006

J.D. SCHULTZ, Ph.D.
PATENT EXAMINER